PCN13

UNDERSTANING QALY GAINS ACROSS DIFFERENT TYPES OF CANCERS AND CANCER-RELATED INTERVENTIONS

Thorat T[1], Chambers J[1], Neumann PJ[2]

[1]*Tufts Medical Center, Boston, MA, USA,* [2]*Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, USA*

OBJECTIVES: To determine for which cancers the largest clinical advancements have been made, and to examine the relative health benefits offered by cancer-related interventions. **METHODS:** We used the Tufts Medical Center Cost-Effectiveness Analysis Registry to identify cost-utility analyses (CUAs) pertaining to cancer-related interventions published from 2002 through 2012. We determined the number of CUAs published for each cancer type, and their geographic setting. We also reported average incremental quality-adjusted life-year (QALY) gain for the five most studied cancer types, and for each cancer type the type of intervention offering largest health gains. **RESULTS:** Of the 3,244 published CUAs, 569 (17%) pertained to cancer. CUAs were most often set in the United States (40%), followed by United Kingdom (15%), Canada (9%) and Netherlands (4%). The five most studied cancers were breast (n=154, 28%), colorectal (n=62, 11%), cervical (n=49, 9%), lung (n=47, 8%) and prostate cancer (n=46, 8%), for which interventions yielded on average, 0.32, 0.32, 0.06, 0.21, 0.22 QALY gains, respectively. Among the five most studied cancers, the largest QALY gains were found for tertiary prevention interventions (mean 0.3, standard deviation (SD) 0.4), e.g., pharmaceuticals and surgeries; followed by secondary prevention (0.2, SD 0.4), e.g., diagnostic imaging. We found primary prevention interventions offered the smallest QALY gain (0.03, SD 0.08), e.g., immunizations. For breast and cervical cancer, pharmaceuticals offered the largest QALY gains, for lung and colorectal cancers, surgeries offered the largest QALY gains; and for prostate cancer, diagnostics offered the largest QALY gains. **CONCLUSIONS:** We found many more CUAs for some cancers than for others, and that cancer-related CUAs are most often set in the US. The magnitude of QALY gain varied by cancer type. Pharmaceuticals offered the largest QALY gains for two of the five most studied cancers, but for other cancer types, surgeries and diagnostic imaging offered the largest QALY gains.

PCN14

COMPARATIVE EFFECTIVENESS OF EVEROLIMUS VS. FULVESTRANT MONOTHERAPY AMONG POSTMENOPAUSAL WOMEN WITH HR+/HER2- METASTATIC BREAST CANCER

Lin PL[1], Hao Y[2], Xie J[3], Li N[1], Ohashi E[1], Koo V[1], Wu EQ[1]

[1]*Analysis Group, Inc., Boston, MA, USA,* [2]*Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA,* [3]*Analysis Group, Inc., New York, NY, USA*

OBJECTIVES: Clinical evidence supports the use of everolimus-based therapy (EVE) and of fulvestrant monotherapy (FUL) among postmenopausal women with hormone receptor-positive human epidermal growth factor receptor-2 negative (HR+/HER2-) metastatic breast cancer (mBC) whose disease progressed on non-steroidal aromatase inhibitor (NSAI). However, direct evidence was lacking on the comparative effectiveness of these agents. This study compared progression-free survival (PFS) between EVE and FUL in a real-world setting. **METHODS:** This retrospective chart review examined postmenopausal HR+/HER2- mBC patients in community-based oncology practices who received EVE or FUL (index therapy) for mBC as first-line, second-line, or third- or later-lines after NSAI. PFS from index therapy initiation was assessed and compared using Kaplan-Meier analysis and a Cox proportional hazards model adjusting for index therapy line and characteristics at mBC diagnosis and index therapy initiation. **RESULTS:** A total of 192 and 156 patients received EVE or FUL, respectively, in a quota-based sample. EVE patients were less likely to have bone metastases, more likely to have visceral metastases or to have received prior chemotherapy for mBC, and had a shorter duration from initiation of last adjuvant endocrine therapy to mBC diagnosis. No significant PFS difference was observed in the unadjusted analysis. After adjusting for baseline characteristics, EVE patients had significantly longer PFS compared to FUL patients (hazard ratio [HR] = 0.71, 95% CI [0.51, 0.99], p = 0.045). When stratified by treatment line, second-line and third- or later-line EVE patients had significantly longer PFS (second-line: HR = 0.52, 95% CI [0.29, 0.91], p = 0.023; third- or later-lines: HR = 0.48, 95% CI [0.24, 0.93], p= 0.031) than FUL patients of the same treatment line. **CONCLUSIONS:** Among postmenopausal women with HR+/HER2- mBC who progressed on NSAI, the use of EVE was associated with better PFS, particularly on second-, third- and later-lines of treatment.

PCN16

COMPARATIVE EFFECTIVENESS OF HUMAN PAPILLOMAVIRUS VACCINATION AGAINST CERVICAL ABNORMALITIES BY DOSE LEVEL IN A COHORT OF PRIVATELY-INSURED U.S. GIRLS

Bensimon AG[1], Hernan MA[2], Gibson T[3], Fung V[3], Chernew M[3], Landrum MB[4], Newhouse JP[4], Schuster M[3], Hsu J[5]

[1]*Harvard University, Cambridge, MA, USA,* [2]*Harvard T. H. Chan School of Public Health, Boston, MA, USA,* [3]*Harvard Medical School, Boston, MA, USA,* [4]*Harvard University, Boston, MA, USA,* [5]*Associate Professor of Medicine, Boston, MA, USA*

OBJECTIVES: Human papillomavirus (HPV) vaccines prevent infection with the most cancer-causing HPV types. However, many age-eligible girls do not initiate or complete the three-dose regimen. There is limited information on the magnitude of protection provided by partial-vaccination. We sought to empirically estimate the effect of HPV vaccination by dose (0, 1, 2 or 3) on cervical abnormality rates in a screening cohort of privately-insured U.S. girls (N=234,829). **METHODS:** We defined a cohort within the MarketScan Commercial Claims database that included 9-17 year-olds in 2007 (year of vaccine introduction) who began Pap screening during 2008-2013. Follow-up started at subjects' first-ever Pap and ended at abnormality detection or censoring. Treatment group corresponded to doses received before the first screening. We used inverse probability of treatment weighting to adjust for birth year, age/year of first Pap and first dose, plan type, region, zipcode-level socioeconomic factors, and claims-based sexual risk proxies. Weighted pooled logistic regressions estimated the effect of dose level on abnormality rates. **RESULTS:** Subjects received zero (63%), one (8%), two (9%), or three (20%) doses (mean ages at first Pap and first dose: 17.8 and 15.6 years). Adjusted incidences of any cytological abnormality (events per 100 annual person-visits) ranged between 11.61 with zero doses and 9.10 with three doses. Incidence rate ratios (IRRs) versus zero doses were 0.91 (95% CI: 0.87-0.96), 0.83 (95% CI: 0.80-0.87), and 0.76 (95% CI: 0.74-0.79) for one, two, and three doses, respectively. For histology-confirmed high-grade lesions (CIN2+), IRRs versus zero doses were 0.63 (95% CI: 0.51-0.77), 0.68 (95% CI: 0.58-0.82), and 0.47 (95% CI: 0.40-0.55) with one, two, and three doses, respectively. **CONCLUSIONS:** HPV vaccination may substantially reduce the risk of cervical abnormalities in real-world settings, even when vaccination is incomplete. Policy and clinical efforts should focus on encouraging eligible girls to initiate vaccination.

PCN17

PREDICTING PHASE III SURVIVAL OUTCOMES USING PHASE II TRIAL DATA IN NSCLC AND RCC

Macaulay R, Tan H

PAREXEL, London, UK

OBJECTIVES: Over 50% of oncology drugs fail in Phase III clinical trials. It remains imperative to better define ways of predicting whether a drug will demonstrate benefits prior to embarking on Phase III clinical trials. This research aims to explore whether Overall Response Rates (ORRs) from Phase II trials can be predictive of Phase III trial outcomes. **METHODS:** Phase III data of any Non-Small Cell Lung Cancer (NSCLC) and Renal Cell Carcinoma (RCC) oncologic appraised by the FDA, or that had failed Phase III clinical trials, since 2002 was extracted along with its corresponding Phase II data. **RESULTS:** 28 oncologics were identified with both Phase II and III readouts (NSCLC: 18, RCC: 10) only 12 (43%) of which met their Phase III trial endpoint (NSCLC: 6/18 (33%), RCC: 6/10 (60%)). Phase II ORRs varied from 0%-61% (mean 26%) and were comparable, on average, to those seen in their corresponding Phase III trials (29%). 7/10 (70%) drugs with Phase II ORRs >30% met their primary endpoint vs. only 5/18 (28%) with ORRs ≤30%. This threshold is dependent on whether the Phase III trial is active or placebo-controlled. For active-controlled Phase III trials, 3/4 (75%) met their primary endpoint with Phase II ORRs >42% vs. 3/12 (25%) with ORRs ≤42%. For placebo-controlled Phase III trials, 3/3 approved with Phase II ORRs >16% versus only 3/9 with ORRs ≤16%. **CONCLUSIONS:** The magnitude of ORRs seen in Phase II can be correlated with later Phase III trial success in NSCLC and RCC. A higher Phase II ORR threshold applies where comparative benefits need to be shown over an active comparator in Phase III as opposed to over placebo. Further research can better define if such thresholds apply to other tumor types and whether this threshold can predict future Phase III trial failures and successes.

PCN18

URSODEOXYCHOLIC AND CHENODEOXYCHOLIC ACID EXERT DISTINCT CYTOTOXIC EFFECTS ON COLON CANCER CELLS

Pavlovic N[1], Stankov K[2], Stanimirov B[1], Stojancevic M[1], Kojic V[3], Bogdanovic G[3], Mikov M[1]

[1]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia and Montenegro,* [2]*Clinical Center of Vojvodina, Novi Sad, Serbia and Montenegro,* [3]*Oncology Institute of Vojvodina, Novi Sad, Serbia and Montenegro*

OBJECTIVES: Hydrophobicity is the most important determinant of toxicity of bile acids (BAs) and depends on the number, position and orientation of hydroxyl groups. Ursodeoxycholic acid (UDCA) is a hydrophilic dihydroxy BA, which is formed by 7β-epimerization of chenodeoxycholic acid (CDCA) in the gut by intestinal bacteria. Unlike the other secondary BAs, UDCA exerts antiapoptotic effects by preventing oxidative stress. The aim of our study was to analyze the influence of stereochemistry of hydroxyl groups on antiproliferative activity of BAs. **METHODS:** Human colon adenocarcinoma HT-29 cells were used to assess the cytotoxicity of CDCA and UDCA using colorimetric MTT assay. In order to explain obtained results of MTT assay, 12 molecular descriptors relevant to polarity, solubility and membrane transport were calculated from 3D structures of CDCA and UDCA using VolSurf+ software. **RESULTS:** Studied BAs displayed distinct degrees of cytotoxicity towards HT-29 cancer cells in a concentration-dependent manner. Concentrations of CDCA and UDCA that inhibited cell growth by 50% (IC50) were 19.6 μM and 351.9 μM, respectively. Oxidative stress is considered to be the most plausible mechanism of cytotoxicity of BAs, which is determined mostly by their hydrophobicity. Calculated molecular descriptor that may explain these distinct cytotoxic effects is amphiphilic moment (A), which is defined as a vector pointing from the centre of hydrophobic domain to the centre of hydrophilic domain. The vector length (5.62 of CDCA and 4.87 of UDCA) determines the ability of compound to permeate a membrane. This was additionally substantiated with the values of CACO2, SKIN and LgBB descriptors that indicate higher Caco-2 permeability, skin permeability and blood-brain barrier distribution of CDCA in comparison to UDCA. **CONCLUSIONS:** More pronounced antiproliferative activity of CDCA in comparison to UDCA was observed. We suggest that computational methods exploring the physicochemical properties of molecules may help in prediction of their cytotoxicity.

PCN19

COMPARING THE EFFICACY OF DENOSUMAB VERSUS ZOLEDRONIC ACID (ZA) FOR PREVENTION OF SKELETAL-RELATED EVENTS (SRES): A CRITICAL APPRAISAL OF THREE PIVOTAL TRIALS

Strite S[1], Stuart ME[2], Beckman V[3], Öhrling K[3]

[1]*Delfini Group, LLC, Portland, OR, USA,* [2]*Delfini Group, LLC/UW School of Medicine, Seattle, WA, USA,* [3]*Amgen Inc., Thousand Oaks, CA, USA*

OBJECTIVES: Rigorous critical appraisal of clinical trials to assess bias and chance effects, which can distort trial results, can help evaluate the validity of research findings. In a pre-specified integrated analysis of three phase 3 pivotal trials in patients with bone metastases secondary to breast cancer, prostate cancer, and other solid tumors or multiple myeloma (N=5,723), denosumab was reported to be superior to ZA for the prevention of SREs, with statistically and clinically significant differences. Delfini Group performed critical appraisals of the three individual pivotal trials and the integrated analysis. **METHODS:** Published trials (Lipton et al, EJC, 2012; Stopeck et al, JCO, 2010; Henry et al, JCO, 2011, Fizazi et al, Lancet, 2011) were analyzed along